

Remarks

Claims 22-27 and 29-31 were pending.

Claims 23, 25, 27 and 30 are cancelled.

Claim 26 is presently withdrawn.

Claims 22, 26, 29, 31 and withdrawn claim 26 are amended.

Claim 24 is as previously presented.

The application now contains claims 22, 24, 29, 31 and withdrawn claim 26.

Claim 22 is amended limit R₁ to methyl and to delete C₁-C₈alkyl from the definition of R₃ and R₅. Claim 22 is further amended to specify that when R₂ is C₁-C₁₂alkyl then one of R₄ and R₆ is C₁-C₂₀alkyl and the other is mono- or di-alkylamino alkyl or -(CH₂)₂-(O-(CH₂)₂)₁₋₄-NH₂; whereas when R₂ is hydrogen one of R₃ and R₅ is hydrogen, one of R₄ and R₆ is C₁-C₂₀alkyl and either R₃ and R₄ or R₅ and R₆ together form a pyrrolidine, piperidine or morpholine ring. Support is inherent in the claims and further support is found at the bottom of page 1 of the specification and in the Examples.

Withdrawn claim 26 is amended to limit R₄ to C₁-C₁₂alkyl and R₆ to -(CH₂)₂-(O-(CH₂)₂)_{1,2}-NH₂.

Claim 29 is amended to limit R₁ methyl, R₂ to hydrogen and to specify that one of R₃ and R₅ is hydrogen, one of R₄ and R₆ is C₁-C₁₂alkyl, and either R₃ and R₄ together or R₅ and R₆ together, form a pyrrolidine or piperidine ring.

Claim 31 is amended to delete the first two structures.

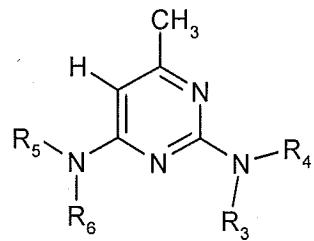
Support is inherent in the claims. No new matter is added.

Rejections

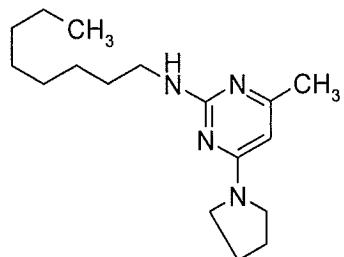
Claim 22-24, 29 and 31 are rejected under 35 USC 103(a) as being obvious over Sunley et. al., US 4,116,674 and Ghoniem et. al., J. Indian Chem Soc, 1986, p 914-917.

Applicants respectfully traverse the rejections.

Applicants have amended the claims to focus on particular aspects of the invention, that is, a method which uses one of two subsets of compounds, subset one being compounds of the formula

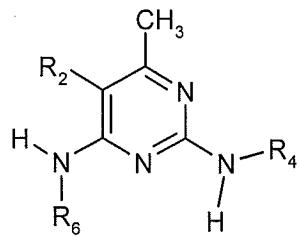


wherein one of the pairs R₃ and R₄ or R₅ and R₆ a saturated cyclic amine and the other pair constitutes a hydrogen and an alkyl, such as

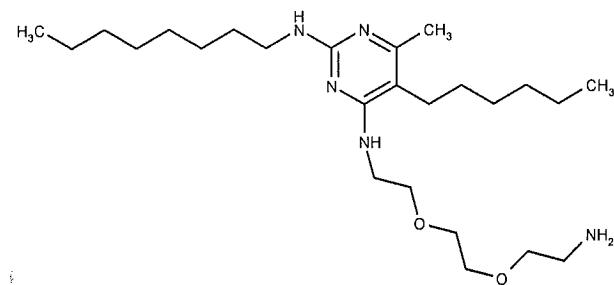


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the subset two being compounds of the formula



wherein R₂ is alkyl one of R₄ and R₆ is alkyl and the other is mono- or di-alkylamino alkyl or -(CH₂)₂-(O-(CH₂)₂)₁₋₄-NH₂ such as



Applicants respectfully note that in the first subset a saturated cyclic amine and a mono-alkyl amine are bound to a 6-methyl pyrimidine. Such compounds are not found in Ghoneim. Further, in the first subset of the instant compounds, the R₂ position is hydrogen. Thus the instant compounds of which comprise a saturated cyclic amine and mono-alkyl amine substituents (subset one) are specifically tri-substituted pyrimidines. Sunley specifically discloses three sub classes of pyrimidines, (two of which bear alkoxy substituents), and the only sub class of Sunley bearing two amino substituents also bears an additional alkyl group at instant position 2, (Sunley col 3 beginning with line 2 and compounds number 36-55). That is, the di-amino substituted pyrimidines of Sunley are tetra substituted.

Applicants respectfully point to the data found on pages 25-27 of the instant specification, the corresponding structures are found on pages 5-11 of the specification. In particular Applicants point to the compounds of subset one bearing a saturated cyclic amine, i.e., PY 10, 15, 24, 31, 36, 44, 51, 67 and 73. In general, these compounds demonstrate good to excellent activity against *Staphylococcus aureus* (sa) and *Corynebacterium xerosis* (CE), except for PY 24 which bears a dialkyl amino substituent and PY 51 which is substituted by phenyl. Thus, 6-alkyl pyrimidines substituted by a saturated cyclic amino and an alkyl amino group perform favorably compared with other classes of pyrimidines when tested against sa and cx.

<u>Compound of formula</u>	<u>MIC sa</u>	<u>MIC ec</u>	<u>MIC cx</u>
PY10	8	>120	<3.75
PY15	15	>120	7
PY24	>120	>120	16
PY31	<3.75	>120	<3.75
PY36	<3.75	>120	<3.75
PY44	<3.75	30	<3.75
PY51	>120	>120	<3.75
PY67	<3.75	>120	<3.75
PY73	18	18	<3.75

However, only PY 44 and PY 73 demonstrate good activity against *Escherichia Coli* (ec), and in fact, these two compounds are among the most effective compounds overall. Applicants note that PY 10 and 31 bear an additional alkyl group at R2, that is they are tetra substituted as found in Sunley. PY 15 is substituted by an aryl amine as found in Ghoneim and 67 bears a t-butyl group at R1. Applicants note that PY 73 is not as effective as PY 44 against sa, most likely due to the presence of the t-butyl group. PY 73 is therefore not included in the instant claims.

In considering the data, Applicants respectfully submit that the compounds of subset one are shown to be among the most active compounds tested across the three bacteria discussed, are more effective than compounds such as those found in Sunley or Ghoniem, and nothing in Sunley or Ghoniem would direct one to this particular group of compounds.

In the compounds of instant subset two, one of the amino groups are substituted by mono- or di-alkylamino alkyl or -(CH₂)₂-(O-(CH₂)₂)₁₋₄-NH₂. Again none of the instant compounds are found in Sunley or Ghoniem. It was also found that when this particular substituent is present, the best results are obtained when the other amino substituent is substituted by one alkyl group and one hydrogen, and, the position R₂ bears an additional alkyl group, i.e., the compounds are tetra substituted.

The table below, lists the data from some of the most active remaining pyrimidines tested. Applicants respectfully point out that only the three highlighted compounds, PY 33, PY 55 and PY 65, which meet all the requirements of subset two, perform as well against each of the three bacteria as PY 44. All others the others fail to meet at least one of the limitations of the instant claims and all the other compounds are inferior against at least one of the three bacteria.

<u>Compound of formula</u>	<u>MIC sa</u>	<u>MIC ec</u>	<u>MIC cx</u>
PY9	5	37	<3.75
PY12	32	64	<3.75
PY19	32	8	8
PY30	16.5	>120	16.5
PY33	<3.75	9.75	<3.75
PY35	17	34	8.5
PY47	<3.75	35	<3.75
PY52	9.25	9.25	<3.75
PY54	<3.75	36	<3.75
PY55	<3.75	<3.75	<3.75
PY56	18.5	9.25	<3.75
PY63	8.75	>120	<3.75
PY65	<3.75	<3.75	<3.75
PY72	31	15.5	<3.75
PY74	34	>120	8.5

Applicants respectfully submit that the compounds of the instantly amended claims demonstrate superior activity against a range of bacteria than other similar compounds. While Ghoniem and Sunley disclose compounds similar to those of the instant claims, Applicants respectfully aver that there is no guidance in either piece of art directing one to the surprisingly higher and more consistent activity of the compounds of the instantly claimed method. That is, neither Sunley or Ghoniem specifically disclose the instantly claimed compounds nor do they suggest the significant difference in activity that was found. Applicants thus respectfully submit that the limited scope of the compounds claimed in the instant method demonstrate superior activity that must be considered unexpected in light of the cited art.

Applicants therefore respectfully submit that the rejections under 35 USC 103(a) over Sunley et. al., US 4,116,674 and Ghoniem et. al., J. Indian Chem Soc, 1986, p 914-917 are addressed and are overcome and kindly ask that the rejections be withdrawn and that claims 22, 24, 29 and 31 be found allowable.

Applicants further kindly ask that upon finding claims 22, 24, 29 and 31, which specifically encompass the elected species, allowable, that the Examiner rejoin claim 26 and also it allowable.

In the event that minor amendments will further prosecution, Applicants request that the examiner contact the undersigned representative.

Respectfully submitted,



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